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EXAMINER	
SULLIVAN, DANIEL M	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,911	NODA ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *12-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/04,9/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: US/10-500-911-2.rag

DETAILED ACTION

This is the First Office Action on the Merits of the application filed 8 July 2004 as the US National Stage of international application 10/500,911, which claims benefit of Japanese application 2002003769 filed 10 January 2002. The preliminary amendments filed 8 July 2004 and 29 July 2004 have been entered. Claims 1-37, as originally filed, are pending.

Election/Restrictions

Applicant's election of Group I, claims 1-11, in the reply filed on 24 July 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 12-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the 24 July reply.

Information Disclosure Statement

The information disclosure statement filed 1 September 2006 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because it is unsigned. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements

based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Objections

Claims 5 and 10 are objected to because of the following informalities:

In claim 5, it is believed that the phrase, "Egr-1 depending renal disease" should read, "Egr-1 dependent disease.

In claim 10, the phrase "under the control of transcriptional control by a protein" is grammatically incorrect.

Appropriate correction is required.

Claim Rejections - 35 USC § 112/101 "use" claims

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6 provide for the use of a protein, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

The claims are directed to methods of using a protein comprising "the same or substantially the same amino acid sequence as that represented by SEQ ID NO: 1 [or 2]" in a method of screening for a prophylactic and therapeutic substance for diseases associated therewith. With regard to polypeptides comprising "substantially the same amino acid sequence", the specification states that the limitation encompasses amino acid sequences having at least about 50% homology to the amino acid sequence represented by SEQ ID NO: 1. (P. 8, ll. 10-15.) With regard to an amino acid sequence "represented by" SEQ ID NO: 1, the application includes no definition of the scope of a sequence "represented by" a defined sequence. Therefore, the limitation is construed as encompassing representation in any way[1] (e.g., having some structural similarity, having the same functional properties, etc.).

Thus, the claims embrace a method of using any protein with a broad and diverse genus to screen for a prophylactic and therapeutic substance for any disease associated in any way with the protein.

The Guidelines for Written Description state "The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art" (Federal Register/ Vol. 66, No. 4/Friday, January 5, 2001/Notices, column 1, page 1105). The Guidelines further state, "[t]he claim as a whole, including all limitations found in the preamble, the transitional phrase, and the body of the claim, must be sufficiently supported to satisfy the written description requirement" (at page 1105, center column, third full paragraph). An

[1] If it is Applicant's intention that claims reciting "the amino acid sequence represented by SEQ ID NO: 1" be limited to amino acid sequences comprising the recited sequence it is recommended that standard claim language (e.g., comprising) be used instead of "represented by".

applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations. *Lockwood v. American Airlines Inc.* (CA FC) 41 USPQ2d 1961 (at 1966).

In the instant case, the protein of the claims is clearly a critical element of the claimed method as it is the only defined element used in the method. Therefore, the polypeptide of the claims must be described according to the requirements of 35 USC § 112, first paragraph.

The Guidelines for Written Description state: "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus" (Federal Register, Vol. 66, No. 4, Column 3, page 1106). "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus" (MPEP §2163(3)(a)(ii)).

In the instant case, the application discloses a polypeptide comprising SEQ ID NO: 2—the human Egr-1 polypeptide known in the art—and a region within SEQ ID NO: 2 that is conserved among mice, rats and humans (i.e., SEQ ID NO: 1). These species are not representative of the broad genus of the claims because they do not convey the necessary common attributes of any polypeptide having 50% identity with those sequences or "represented by" those sequences and useful in a method of screening for a prophylactic and therapeutic substance for a disease associated with the protein. In addition to the disclosed species, the application also provides generic guidance on producing "muteins", however, the guidance

provided does not amount to a description of the protein of the claims because there is no disclosure of which muteins within the scope of "substantially the same amino acid sequence as that represented by SEQ ID NO: 1" can be used in a screening method for a prophylactic and therapeutic substance for a disease associated with the protein.

Although the application discloses some methods with which one might test polypeptides for the requisite activity, an adequate written description of a polypeptide requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the polypeptide itself. It is not sufficient to define polypeptide solely by its principal biological property because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any polypeptide with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all polypeptides that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). With respect to method claims, adequate description of the methods first requires an adequate description of the materials, i.e. specific DNA sequences, which provide the means for practicing the invention.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of any polypeptide comprising substantially the same amino acid sequence as that

represented by SEQ ID NO: 1 and useful in a method of screening for a prophylactic and therapeutic substance associated therewith. Therefore, only the described polypeptides comprising SEQ ID NO: 1 or SEQ ID NO: 2 meet the written description provision of 35 U.S.C. §112, first paragraph.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims: The claims are directed to methods of using a protein comprising "the same or substantially the same amino acid sequence as that represented by SEQ ID NO: 1 [or 2]" in a method of screening for a prophylactic and therapeutic substance for diseases associated therewith. As described above, the polypeptide of the claims is broadly drawn and, therefore, so too is the scope of the method of screening for a prophylactic and therapeutic substance for any disease associated with the protein. In other words, as the

polypeptide of the claims embraces structurally and functionally diverse proteins, the method of the claims embraces screening for prophylactic and therapeutic substances for a wide variety of diseases.

In addition, even claims more narrowly drawn to screening for a prophylactic and therapeutic substance for renal disease or diabetic nephropathy cover the use of a wide variety of structurally and functionally diverse polypeptides in the method. Similarly, even if one were to construe claims limited to using an amino acid sequence represented by the recited sequence as requiring that the method use a polypeptide that comprises the recited sequence, the claims still embrace methods of identifying prophylactic and therapeutic substances for *any* disease associated with the protein.

State of the prior art and level of predictability in the art: The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability.

The physiological art is recognized as unpredictable. (MPEP 2164.03.) In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In

cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

In the instant case, the claims are directed to using the polypeptides of the claims as a marker for efficacy in the treatment of any disease associated in any way with the polypeptide. In that regard, the art teaches that before a putative biomarker can be used as a surrogate endpoint it must be validated as such. Wagner (2002) *Dis. Markers* 18:41-46 acknowledges in the Abstract, "Putative biomarkers are typically identified because of a relationship to known or hypothetical steps in a pathophysiologic cascade. Biomarker discovery can also be effected by expression profiling experiment using a variety of array technologies and related methods." However, Wagner cautions, "A rational basis for recommending the use of a putative biomarker does not guarantee the utility of the biomarker or its qualification as a surrogate endpoint" (paragraph bridging the left and right columns on page 43) and "Biomarkers require validation in most circumstances" (paragraph bridging pages 43-44).

Frank *et al.* (2003) *Nature Rev.* 2:566-580 concurs, stating, "The standard concepts of test-re-test reliability and validity apply with equal force to clinical biomarkers as they do in any assay system" and, "The work required to establish the reliability and validity of a new biomarker should not be underestimated in general, and in particular needs of planning for each combination of clinical indication and mechanism of action" (paragraph bridging the left and right columns on page 568). Feng *et al.* (2004) *Pharmacogenomics* 5:709-719 teaches, "The development and validation of clinically useful biomarkers from high-dimensional genomic and proteomic information pose great research challenges. Present bottle necks include: that few of

the biomarkers showing promise in initial discovery were found to warrant subsequent validation...A molecular profiling approach, although promising, has a high chance of yielding biased results and overfitted models" (Abstract).

Viewed as a whole, the art clearly teaches that the utility of a putative biomarker as an indicator of prophylactic and therapeutic efficacy is unpredictable and must be validated.

Amount of direction provided by the inventor and existence of working examples: It is first noted that, with the exception of renal disease, all of the teachings in the application directed to diseases for which the instant method can provide an effective prophylactic and therapeutic substance are generic. The application states, "The diseases associated with the protein of the present invention include diseases in which the amount of the protein of the present invention is increased or decreased when comparing with that of the normal time." However, the application provides no evidence that all diseases in which the protein of the claims is increased or decreased can be prevented and treated using a compound identified by the claimed method.

With regard to renal disease, the application discloses that expression of Egr-1 increased in diabetic Wistar fatty rats (Example 1), diabetic Zucker fatty rats (Example 2), rat glomerular mesangial cells exposed to serum (Example 3), and spontaneously hypercholesterolemic rats (Example 4). The application also shows that overexpression of Egr-1 protein in a kidney cell line results in expression of fibrosis-related genes (Example 5) and that induced expression of Egr-1 can be inhibited by an angiotensin II receptor antagonist in the Zucker fatty rat (Example 2) and rat mesangial cells (Example 3) and by an Egr-1 antisense oligonucleotide in cultured mesangial cells (second "Example 1" beginning on page 74).

The application asserts, "The present inventors... have for the first time found out that the expression of renal Egr-1 in a renal disease model animal is remarkably increased, and further for the first time that suppression of the expression of renal Egr-1 in a renal disease model animal can produce a therapeutic effect on a renal disease. The present inventors have further carried out studies based on findings thereof, thus leading to the completion of the present invention." However, the application clearly does not contain validation of the method as it encompasses screening for a prophylactic and therapeutic substance that can be used to treat any disease associated with the protein of the claims (i.e., wherein expression of the protein is increased or decreased). In addition, with regard to renal disease, the application appears to contain only data showing altered expression of Egr-1 in certain disease models, which the art does not recognize as sufficient to establish that the protein is a valid surrogate endpoint for identifying therapeutic and prophylactic agents. Contrary to Applicant's assertion, there does not appear to be any evidence presented demonstrating that an agent that alters the expression or function of Egr-1 produces a therapeutic effect in a disease model.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, the skilled artisan would not be able to use the claimed invention to identify a prophylactic and therapeutic substance for diseases associated with the protein of the claims without first having to engage in undue experimentation to establish that the expression or function of the protein is a valid marker for disease and response to a substance capable of preventing and treating that disease. The art clearly establishes that putative biomarkers must be validated and that "few of the biomarkers

showing promise in initial discovery were found to warrant subsequent validation" (Feng *et al.*, *Id.*).

Given this high degree of unpredictability and the absence of evidence demonstrating that expression or function of the protein of the claims is a valid surrogate endpoint for therapeutic efficacy in any disease associated with the protein, the basic premise underlying the claimed invention is no more than a theoretical possibility. This is not sufficient to meet the enablement requirement of 35 USC §112, first paragraph.

> Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. *Genentech Inc. v. Novo* Nordisk A/S (CA FC) 42 USPQ2d 1001, 1005.

In view of the foregoing, it would require undue experimentation to practice the invention claimed. Therefore, the claims are properly rejected under 35 USC §112, first paragraph, as lacking an enabling disclosure.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 10 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7 and 11 are indefinite because the claims require "comparing production of a protein or salts thereof comprising the same or substantially the same amino acid sequence as that represented by SEQ ID NO: 1" but do not specify what is being compared. Although the claims also recite, "in the case where a cell is cultivated that has the capability of producing the protein or salts thereof and the case where the cell is cultivated in the presence of a test compound", there is nothing in the claims to indicate that it is results obtained under those conditions that are compared. Therefore, it is unclear what is covered by the claim scope. In the interest of compact prosecution, the claims will be examined with the assumption that the activity in a cell cultivated in the absence of a test compound is compared with the cell cultivated in the presence of a test compound as is believed to be the intended meaning of the claims.

Claim 10 is indefinite in reciting, "the activity is an expression-controlling activity of a gene under the control of transcriptional control by a protein or salts thereof comprising the same or substantially the same amino acid sequence as that represented by SEQ ID NO: 1". It is unclear what activity is being measured. The expression of a gene under the transcriptional control of the SEQ ID NO: 1 protein? The regulation of a gene under the transcriptional or translational control of a gene that is itself regulated by the SEQ ID NO: 1 polypeptide? In the interest of compact prosecution, the claim will be examined according to its broadest reasonable scope as reading on a method wherein the expression of a gene under the transcriptional control of the SEQ ID NO: 1 protein is measured.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by any one of Rosenberg (1993) *Kidney Int.* 43:601-609, Rupprecht et al. (1993) *Am. J. Physiol.* 265:F351-F360 (hereinafter, Rupprecht '93), or Kim et al. (1995) *Circulation* 92:88-95 (made of record in the IDS filed 8 July 2004).

The claims are directed to a screening method for a prophylactic and therapeutic substance for diseases associated with a protein or salts thereof comprising the same or substantially the same amino acid sequence as that represented by SEQ ID NO: 1, which is characterized by using the protein or salts thereof. The dependent claims further recite that the protein has the amino acid sequence represented by SEQ ID NO: 1 or 2 and that the disease is a renal disease, which might be an egr-1 dependent disease or diabetic nephropathy. As described above, the sequence limitations of the claims are read broadly and are construed as covering, at a minimum, any polypeptide recognized as Egr-1[2]. With regard to the intended use (i.e., screening for a prophylactic and therapeutic substance for diseases associated with a protein), the application does not point out any steps that must be comprised by the method of screening and

[2] Although the claims as written do not require the use of a polypeptide comprising a specific sequence, it is noted for the record that the instant SEQ ID NO: 2, which comprises SEQ ID NO: 1, was known in the art many years prior to the filing of the instant application. (See, e.g., the attached sequence alignment us 10-500-911-2.rag.)

the discussion commencing at page 28, line 17 indicates that any method wherein the effect of an agent on the expression or function of the protein is determined is within the scope of the claims.

Rosenberg et al. teaches comparing expression of Egr-1 mRNA in rat kidney (an indirect measure of protein expression) with and without infusion of various agents including norepinephrine, angiotensin II and angiotensin II with angiotensin II antagonist. (See especially the paragraph bridging pp. 603-604, the first full paragraph on p. 604, and Table 4.) The method of Rosenberg et al. is the same as the method claimed in the instant application.

Rupprecht '93 compares the production of Egr-1 mRNA in cultured mesangial cells in the absence of a test compound (i.e., PDGF only) to the production in the presence of a test compound (genistein). (See especially Figure 1.) The method of Rupprecht '93 is the same as the method presently claimed.

Kim et al. compares the production of Egr-1 mRNA in carotid artery in the absence of a test compound (i.e., balloon injury only) to the production in the presence of a test compound (i.e., the angiotensin II receptor antagonist TCV-116). (See especially the section entitled "Effects of TCV-116 on Expression of Immediate-Early Genes and ODC", Figure 2 and the caption thereto.) The method of Kim et al. is the same as the method presently claimed.

Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by any one of Hofer et al. (1996) *J. Biol. Chem.* 271:28306-28310, Rupprecht et al. (1997) *Kidney Int.* 51:694-702 (hereinafter, Rupprecht '97), or Khachigian et al. WO 97/32979 (made of record in the IDS filed 8 July 2004).

The limitations of claims 1-6 are described herein above. Claim 7 is construed as additionally requiring that the production of protein in the presence and absence of a test compound be compared.

Hofer et al. compares the production of Egr-1 protein by cultured mesangial cells in the absence of a test compound to the production in the presence of various test compounds. (See especially Figures 1, 3, 4 and 7.) The method of Hofer et al. is the same as the method presently claimed.

Rupprecht '97 compares the production of Egr-1 protein by cultured mesangial cells in the absence of a test compound (i.e., PDGF only) to the production in the presence of various test compounds (i.e., antisense oligonucleotides). (See especially Figure 4 and the caption thereto.) The method of Rupprecht '97 is the same as the method presently claimed.

Likewise, Khachigian et al. compares the production of Egr-1 protein by cultured mesangial cells in the absence of a test compound (i.e., serum only) to the production in the presence of a test compound (i.e., various antisense oligonucleotides). (See especially p. 15, ll. 19-34.) The method of Khachigian et al. is the same as the method presently claimed.

Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by any one of Einstein et al. WO 01/04356 A1 or Alberini et al. WO 01/74298 A2 (both made of record in the IDS filed 8 July 2004).

The limitations of claims 1-7 are described herein above. Claim 8 is directed to the method of claim 1 comprising comparing an activity of the protein in the presence and absence

of a test compound, claim 9 limits the compared activity to a binding activity to a polynucleotide and claim 10 limits the activity to expression controlling activity.

Einstein et al. teaches methods of identifying agents that modulate the activity of an Egr-1 protein including comparing protein expression in the presence and absence of a test compound (see, e.g., paragraph bridging pp. 15-16), the ability of the protein to bind to its binding site on a nucleic acid or the transactivation of a gene product regulated by the Egr-1 protein (see especially p. 15, l. 21 through p. 16, l. 3 and p. 17, ll. 10-20). The method of Einstein et al. is the same as the method presently claimed.

Alberini et al. teaches methods of identifying agents that modulate the activity of an Egr-1 protein (referred to therein as ZIF268) including comparing the ability of the protein to bind to its binding site on a nucleic acid or the transactivation of a gene product regulated by the Egr-1 protein in the presence and absence of a test compound. (See especially p. 17, first and second full paragraphs and P. 24, ll. 7-19.) The method of Alberini et al. is the same as the method presently claimed.

Claims 1-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Rupprecht et al. (2000) *Kidney Int.* 57:70-82 (hereinafter, Rupprecht '00).

The limitations of claims 1-10 are described herein above. Claim 11 is directed to the method of claim 1 wherein the method comprises comparing the production of a protein and a binding activity of the protein to a polynucleotide using the polynucleotide and an antibody against the protein.

Rupprecht '00 teaches a method comprising comparing the expression of an Egr-1 protein in the absence (i.e., serum only) and presence of a test compound (i.e., GSNO or 8Br-cGMP). (See especially Figures 5 and 6 and the captions thereto.) In addition, Rupprecht '00 teaches a method comprising comparing expression of a reporter gene under the transcriptional control of Egr-1 in the absence and presence of a test compound. (See especially Figure 9 and the caption thereto.) Finally, Rupprecht '00 teaches a method comprising comparing binding of Egr-1 to a polynucleotide comprising the Egr-1 binding site wherein the method uses the polynucleotide and an antibody against Egr-1 (i.e., supershifting). See especially Figures 7 and 8 and the captions thereto. The method of Rupprecht '00 is the same as the method claimed in the instant application.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M. Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Art Unit 1636